

**Amendment and Response**

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Serial No.: 09/600,432

Confirmation No.: 3387

Filed: October 2, 2000

For: PEPTIDES WITH  $\beta$ 1 INTEGRIN SUBUNIT DEPENDENT CELL ADHESION MODULATING ACTIVITY**Remarks**

The Office Action mailed May 8, 2003 has been received and reviewed. Claims 6-11 having been amended, claims 23-28 currently withdrawn from examination, and claims 29-36 having been added, the pending claims are claims 6-11, 23-36. Reconsideration and withdrawal of the rejections are respectfully requested.

Support for amended claims 6-11 is found original claims 1 and 7-11. Support for the new claims is found throughout the specification. For example, support for new claims 29-36 is found at page 2, lines 10-11; page 2, line 14; and page 8, lines 21-22 and in original claims 6, 7, 11, 12, and 15. No new matter has been added.

**Request for Rejoinder under 37 CFR §1.121**

Claims 23-28, directed to a process for using a product, were previously withdrawn from examination pursuant an election filed in response to the Restriction Requirement mailed February 19, 2002. Claims 23-28 include all the limitations of the examined product claims. Pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86), withdrawal of the restriction requirement, and rejoinder and examination of the previously withdrawn claims 23-28 is respectfully requested.

**The 35 U.S.C. §112, Second Paragraph, Rejection**

The Examiner rejected claims 7-11 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed. Applicants submit that the amendments to claims 7-11, to clarify the claimed invention, render this rejection moot. Withdrawal of this rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

**The 35 U.S.C. §102 Rejection**

The Examiner rejected claims 6-11 under 35 U.S.C. §102(b) as being anticipated by Newsholme et al. (*Journal of Biological Chemistry* 267(2), 810-818, 1992), Ohba (U.S. Patent No.

5,359,048), and Westerlink (*Proc Natl Acad Sci* 92, 4-21, 1995). These rejections are respectfully traversed.

Claims 6-11 are drawn to a "peptide of no more than about six amino acid residues, said peptide having the sequence Pro-Arg-Ala-Arg-Ile-Tyr (SEQ ID NO:24), Arg-Ala-Arg-Ile-Tyr (SEQ ID NO:25), Ala-Arg-Ile-Tyr (SEQ ID NO:26), or Arg-Ile-Tyr." Thus, the peptide of claims 6-11 are no more than about six amino acid residues in length.

The Examiner asserted that Newsholme et al. disclose a peptide that is the same as that of claims 6-11. Specifically, the Examiner asserted that the fourth peptide from the last of those shown in the Table 1, page 811 of Newsholme et al. is the same as that claimed. The peptide shown in Newsholme et al. is twenty-five amino acids in length. The claimed peptides are no more than about six amino acid residues in length. Thus, Newsholme et al. do not disclose each and every element set forth in claims 6-11.

The Examiner asserted that Ohba et al. disclose a peptide that is the same as that of claims 6-11. Specifically, the Examiner asserted that the polypeptide that spans columns 17-261 of Ohba et al. is the same as that claimed. The peptide shown in Ohba et al. is 1149 amino acids in length. The claimed peptides are no more than about six amino acid residues in length. Thus, Ohba et al. do not disclose each and every element set forth in claims 6-11.

The Examiner asserted that Westerlink et al. disclose a peptide that is the same as that of claims 6-11. Specifically, the Examiner asserted that the peptide 3 shown in Table 1, p. 4023 of Westerlink et al. is the same as that claimed. The peptide shown in Westerlink et al. is thirteen amino acids in length. The claimed peptides are no more than about six amino acid residues in length. Thus, Westerlink et al. do not disclose each and every element set forth in claims 6-11.

Likewise, neither Newsholme et al., Ohba et al., nor Westerlink et al. disclose each and every element set forth in new claims 29 and 30, drawn to "[a] peptide consisting of the sequence Pro-Arg-Ala-Arg-Ile-Tyr (SEQ ID NO:24), Arg-Ala-Arg-Ile-Tyr (SEQ ID NO:25), Ala-Arg-Ile-Tyr (SEQ ID NO:26), or Arg-Ile-Tyr" and "[a] peptide of no more than about ten amino acid residues, said peptide having the sequence Pro-Arg-Ala-Arg-Ile-Tyr (SEQ ID NO:24), Arg-Ala-Arg-Ile-Tyr (SEQ ID NO:25), Ala-Arg-Ile-Tyr (SEQ ID NO:26), or Arg-Ile-Tyr," respectively.

In addition, the peptides of dependant claims 7-11 and new claims 31-36 include various functional limitations. The peptide of claims 7, 31, 32, 33, and 35 "modulates  $\beta 1$  integrin subunit dependent adhesion," the peptide of claim 8 "inhibits  $\beta 1$  integrin subunit dependent adhesion," the peptide of claim 9 "modulates  $\alpha 4 \beta 1$  integrin dependent adhesion," the peptide of claim 10 "inhibits  $\alpha 4 \beta 1$  integrin dependent cell adhesion," and the peptide of claims 11, 34, and 36 "inhibits  $\alpha 4 \beta 1$  integrin dependent adhesion of Ramos cells to  $\alpha 4 \beta 1$  integrin binding fibronectin fragments." In rejecting claims 7-11 the Examiner asserted that these claims "are anticipated because the recited properties are inherent in the prior art peptide." Applicants respectfully disagree.

In rejecting claims 7-11, the Examiner has based the rejection on the doctrine of inherency. "To establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." M.P.E.P §2112. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." M.P.E.P §2112 (emphasis in original). It is respectfully submitted that the Examiner has not met his burden of providing a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the cited documents.

The claimed peptides modulate  $\beta 1$  integrin subunit dependent adhesion (claims 7, 31, 32, 33, and 35), inhibit  $\beta 1$  integrin subunit dependent adhesion (claim 8), modulate  $\alpha 4 \beta 1$  integrin dependent adhesion (claim 9), inhibit  $\alpha 4 \beta 1$  integrin dependent cell adhesion (claim 10), and inhibit  $\alpha 4 \beta 1$  integrin dependent adhesion of Ramos cells to  $\alpha 4 \beta 1$  integrin binding fibronectin fragments (claims 11, 34, and 36). Applicants note that new claim 35 is the same as original claim 7.

The peptide taught by Newsholme et al. is a peptide fragment of a phosphorylase kinase protein (see Table I of Newsholme et al.). The peptide taught by Ohba et al. is a protein of 1149 amino acid residues, with insecticidal properties, isolated from the bacteria *Bacillus thuringiensis* serovar *japonensis* strain *Buibui* (see col. 3, lines 4-11 of Ohba et al.). And, the peptide taught by

Westerlink et al. is a peptide from the surface exposed regions of the anti-idiotypic antibody 6F9 (see Table 1 of Westerlink et al.).

Newsholme et al., Ohba et al., or Westerlink et al. do not teach peptides that modulate  $\beta$ 1 integrin subunit dependent adhesion, inhibit  $\beta$ 1 integrin subunit dependent adhesion, modulate  $\alpha$ 4 $\beta$ 1 integrin dependent adhesion, inhibit  $\alpha$ 4 $\beta$ 1 integrin dependent cell adhesion, or inhibit  $\alpha$ 4 $\beta$ 1 integrin dependent adhesion of Ramos cells to  $\alpha$ 4 $\beta$ 1 integrin binding fibronectin fragments. And, Applicants respectfully submit that there is no basis in fact and/or technical reasoning to reasonably support a determination that the functional characteristics of the peptides of claims 7-11 are necessarily present in the peptide described by Newsholme et al. (a peptide fragment of a phosphorylase kinase protein), Ohba et al. (an insecticidal protein isolated from the bacteria *Bacillus thuringiensis* serovar *japonensis* strain *Buibui*), or Westerlink et al. (a peptide from the surface exposed regions of an antibody), and that it would be so recognized by persons of ordinary skill. Thus, the peptides of claims 7-11 are not anticipated by the teachings of Newsholme et al., Ohba et al., or Westerlink et al.

As presented above, Applicants respectfully submit that the teachings of Newsholme et al., Ohba et al. and Westerlink et al. do not anticipate claims 6-11. Reconsideration and withdrawal of this rejection of claims 6-11 under 35 U.S.C. §102(b) is respectfully requested. Similarly, the teachings of Newsholme et al., Ohba et al. and Westerlink et al. do not anticipate the peptides of new claims 29-36.

### **Information Disclosure Statement**

The Examiner has stricken JP6016568 from the IDS because of the absence of an English translation. As suggested by the Examiner, Applicants list this document under "other documents" as English Abstract of JP 6016568.

The Examiner has stricken "Seki et al. (Quantitative Analysis of Digestion-Resistant ACE Inhibitor Dipeptides....)" because of the absence of an English translation. As suggested by the Examiner, Applicants list this document as English Abstract of Seki et al. (*J. Jap. Food Sci. Technol.* 43, 967, 1996).

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The Examiner indicates the remaining references were stricken from the IDS because they were not received. Applicants submit herewith the replacement copies of these remaining references.

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**Summary**

It is respectfully submitted that the pending claims 6-11 and 23-36 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

**CERTIFICATE UNDER 37 CFR §1.10:**

The undersigned hereby certifies that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450  
"Express Mail" label number: **EV073737975 US**  
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Respectfully submitted,  
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